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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,009	07/08/2003	Stanley T. Crooke	ISIS-5138	1016
32650	7590	05/25/2006	EXAMINER	
WOODCOCK WASHBURN LLP ONE LIBERTY PLACE - 46TH FLOOR PHILADELPHIA, PA 19103			WOLLENBERGER, LOUIS V	
		ART UNIT	PAPER NUMBER	
		1635		

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/616,009	CROOKE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Louis V. Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 08 July 2003.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1 and 29-74 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) \_\_\_\_\_ is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) 1 and 29-74 are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
    - a) All    b) Some \* c) None of:
      1. Certified copies of the priority documents have been received.
      2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
      3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                    | Paper No(s)/Mail Date. _____.   |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____.                                   |

**DETAILED ACTION**

***Preliminary Amendment***

Applicants' preliminary amendment to the claims, filed on of 7/8/2003, is acknowledged.

With this amendment, claims 1 and 29–74 are pending and subject to restriction as follows.

***Election/Restrictions***

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1, 29–44, 49, and 50, drawn to a mixed sequence antisense oligonucleotide comprising first and further portions, classified in class 536, subclass 24.5, for example. Election of this group requires a further election of a single species of 2' substituent for each of said first and further portions, respectively, recited in claims 33, 34, 36, and 37. Applicant must also further elect a single species of linkage for said further portion, recited in claim 38, as explained below.
- II. Claims 45 and 47, drawn to a mixed sequence antisense oligonucleotide comprising at least 8 nucleotides and having a 2'-OH arabinonucleotide sequence, classified in class 536, subclass 24.5, for example.
- III. Claims 46 and 48, drawn to a mixed sequence antisense oligonucleotide comprising at least 8 nucleotides and having a 2'-F arabinonucleotide sequence, classified in class 536, subclass 24.5, for example.

- IV. Claims 51–68, drawn to a method comprising contacting an oligonucleotide with RNA or DNA *in vitro* or in a cellular assay, classified in class 435, subclass 6, for example.
- V. Claims 69–71 and 74, drawn to a method for identifying and selecting an antisense oligonucleotide, classified in class 435, subclass 6, for example.
- VI. Claims 72 and 73, drawn to an oligonucleotide for modulating a target nucleic acid identified using the process of claim 69, classified in class 536, subclass 24.5, for example.

Inventions I–III and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are drawn to structurally and functionally distinct oligonucleotides that have different designs, and, therefore, different modes of operation and different effects. For example, Groups II and III are drawn to oligonucleotides having either 2'-OH or 2'-F arabinonucleotide sequence, which is not required by either Group I or VI. Group I is drawn to an oligonucleotide having any number of specific 2' substituents and internucleoside linkages, and to an oligonucleotide having a specific conformational geometry, which are not required by Groups II, III, or VI. Group VI is drawn to an oligonucleotide that is specifically identified using the process of claim 69, which process for identifying is not required by any other groups, and which process may identify oligos having specific features and properties distinct from any of the other oligos of Groups I–III.

Accordingly, the different oligonucleotides have different structures and therefore different chemical/physical properties and activities.

Inventions IV and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case the different inventions are unrelated because they are drawn to methods that are distinct both physically and functionally, and are not required one for the other. The different methods require different steps and/or use different molecules. For example, Group IV requires the use of an oligonucleotide as defined by any of claims 29, 32, 33, or 45–50, and requires contacting the oligo with RNA or DNA *in vitro* or in assay, which is not specifically required by Group V. Group V requires an oligonucleotide identified specifically by the process of claim 69, which process encompasses steps for selecting and contacting cells either *in vitro* and *in vivo* and requires measuring specific parameters such as those recited in claim 71, which steps are not specifically required by Group IV.

Inventions I–III are related to invention IV as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the product antisense oligonucleotides can be used in a materially different process. For example, the product antisense oligonucleotides can be used as probes in Northern blotting assays to determine the presence and relative quantity of specific mRNA transcripts, which does not require contacting the nucleic acids with cells or DNA in a cellular assay as in Group IV.

Inventions I–III are unrelated to invention V. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, inventions I–III are drawn to products that are not disclosed as capable of use together with methods for identifying and selecting oligonucleotides according to invention V.

In addition, searching and examining each of these groups in a single application would present a serious burden on the examiner, since each group would require different keyword searches (i.e., different fields of search) and different considerations of the patent and non-patent literature with regard to novelty and unobviousness.

Therefore, because these inventions are distinct for the reasons given above, and the searches required for each are divergent and not coextensive, and because a search and examination of all of the Inventions in a single application would present a serious burden on the Examiner, restriction for examination purposes as indicated is proper.

*Election of Species*

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Group I contains claims directed to the following patentably distinct species:

- Oligonucleotides differing with regard to the type of 2' substituent on the first portion (claims 33 and 34)
- Oligonucleotides differing with regard to the type of 2' substituent on the further portion (claims 36 and 37)
- Oligonucleotides differing with regard to the type of linkage joining the nucleotides of the further portion (claim 38)

Claim 36, in particular, comprises countless numbers of chemically and functionally distinct oligonucleotides, having formula I or II. These formulas alone, notwithstanding the many possible combinations of III and IV that are possible within formulas I and II in any given oligonucleotide compound, encompass an exponential number of structurally and functionally distinct species of oligomeric compounds.

The species listed above are independent or distinct because the species of oligomeric compounds, defined by the various formulas and alternative modifications recited in the claims, have different structures and, therefore, different chemical properties and biological effects. For example, the different species may differ with regard to solubility, cellular uptake, and nuclease

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stability, all of which are expected to contribute to their mode of action in vivo or in vitro. The different species would also differ in their reactivity and the starting materials from which they are made. It is also possible that the method and utility of each species would differ according to the best mode of administration or delivery required for each species and the particular applications each is suited for.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Thus, Applicants must elect a single species of 2' substituent for the first portion and a single 2' substituent and linkage for the further portion, showing all atoms and bonds that are necessary to define said compound. Applicants should not use general notations like R<sub>1</sub> or R<sub>2</sub>, etc. when defining the structure because these labels represent more than one chemical group and thus more than one compound would be erroneously elected. The 2' substituents chosen for each of the first and further portions do not have to be the same, but a single substituent for each portion must be identified by election.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an

allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

### *Rejoinder*

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

### *Conclusion*

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and

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specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

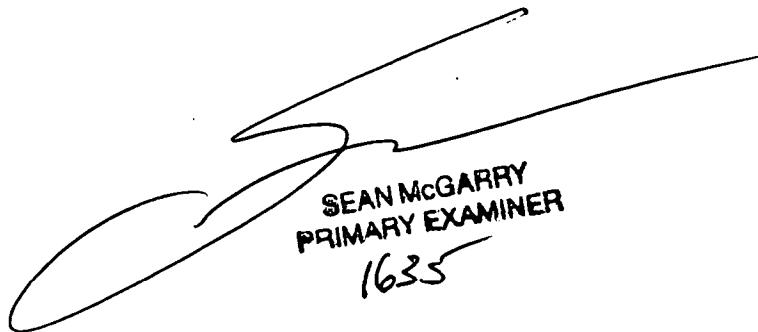
Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571)272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Louis Wollenberger, Ph.D.  
Examiner, Art Unit 1635  
May 11, 2006



SEAN McGARRY  
PRIMARY EXAMINER  
1635